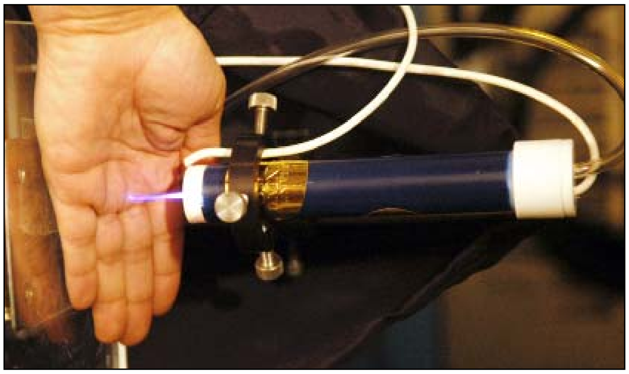
Plasma Medicine

Imagine blowing a cold breeze of helium on a bleeding wound and watching the blood coagulate as the wound starts to heal at a faster rate than it normally would. It sounds far-fetched, but teams of scientists with expertise in plasma science, microbiology, biochemistry, and medicine are working on making something like that actually happen. They do not use helium exactly, but rather helium (or other gases) in an activated state called "plasma."

Plasma is the fourth state of matter. The other three are the solid, the liquid, and the gaseous states. If a gas is heated or subjected to high electric fields, any electrons present are accelerated to high kinetic energies. When these electrons collide with the atoms and molecules of the background gas they are able to knock off and free more electrons. The atoms/molecules missing one or more electrons are called "ions." The newly freed electrons are accelerated by the applied electric field and, in turn, enter into ionizing collisions with other atoms and molecules. The mixture of neutral atoms and molecules, ions, and electrons is what is referred to as "plasma."

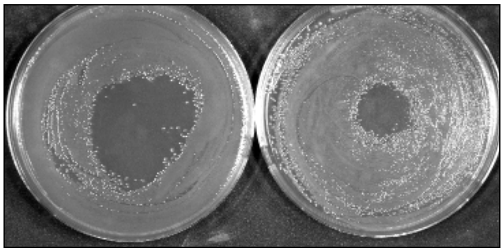


A cold plasma can contact skin without harming it, making it ideal for disinfecting wounds.

Plasmas range in temperature from the very hot (matter at the beginning of the big bang) to the very cold (laboratory condensed matter). Medical plasmas are in the "Goldilocks" range – hot enough to produce the reactive species needed for effective treatment, but cold enough to leave tissue unharmed.

In the last decade, research on the use of low temperature plasmas in medicine have intensified, and today plasmas are poised to dramatically affect healthcare. Researchers have discovered ways that plasmas can be applied directly to living tissues to deactivate pathogens; to stop bleeding without damaging healthy tissue; to disinfect wounds and accelerate wound healing; and to selectively kill some types of cancer cells.

Plasmas produce chemically reactive atoms and molecules such as hydroxyl (OH) and atomic oxygen (O) that can kill harmful bacteria through oxidation. This is important because oxidation of the lipids and proteins that constitute a cell's membrane can lead to the complete disruption of the membrane.



Petri dishes of *E. coli* cells were exposed for 120 seconds to a cold plasma plume (left - helium + 0.75% O_2; right - helium only). The dark zones in the center are "kill zones," where bacterial cells were destroyed and not able to replicate/multiply.

Researchers discovered that bacteria cannot cope with the harsh environment created by plasmas; bacteria died in large numbers in a matter of minutes or even seconds, depending on the strength of the bacterial strain. Scientists have exploited this property of plasma to develop plasma devices that can be used to sterilize medical tools and instruments without the risk of damaging them.

Many modern medical tools are made from polymers that are heat sensitive and therefore cannot be sterilized by conventional means, such as autoclaving, which uses high pressure hot steam. Reactive plasma species sustained near room temperature can rapidly kill bacteria, viruses and fungi deposited on the surfaces of surgical instruments and medical devices, including those made of heat-sensitive polymers. Since these plasma species are often maintained in a gas flow, they can diffuse into structures

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that are narrow and difficult-to-access, characteristics that are increasingly common among instruments for minimally invasive surgeries. These special properties of cold gas plasmas offer the prospect of protection from highly infectious agents such as prion, a structurally misshaped protein that is responsible for "mad cow disease," and which is resistant to all commercial decontamination procedures.

Reactive plasma species appear to cause little or tolerable damage to living animal and plant tissues, while being capable of destroying bacterial cells. This is because bacterial and mammalian cells have very different responses to chemical and physical stresses, such as those experienced with cold gas plasma treatments. Consequently, skin fibroblast cells are found to remain viable under plasma conditions that are lethal to *E. coli* cells. This ability of plasma to destroy bacteria while leaving animal and plant tissue unharmed is key to the development of important plasma applications, including food decontamination, skin disinfection, and tumor reduction.

Similar to chemotherapies, cold plasma treatments appear to be able to induce programmed death (apoptosis) among cancer cells, arresting the rapid proliferation of cancerous cells, but with little damage to living human tissues. Ultimately, the success of this approach will depend on finding the right recipes of reactive plasma species, and delivering them effectively to the complex environment of diseased sites in the human body. There is hope that cold gas plasma applications can be developed to solve some of these pressing medical challenges.

While plasma can destroy pathogens at sufficient doses, at a low dosage it can also accelerate the multiplication of cells, an important step in the wound healing process. The ability of plasma to kill bacteria cells and to accelerate the proliferation of specific healthy tissue cells, known as the "plasma kill/plasma heal" process, has led scientists to investigate the use of cold plasma for wound care. Chronic wounds, such as diabetic ulcers, do not respond well to conventional healing methods. Tens of thousands of amputations occur every year in the US because present medical methods are not able to heal these types of wounds. Although plasma-based technology for wound care is still in the research phase, preliminary tests show signs of successful treatments of some types of chronic wounds.

Plasma can be use to control plaque, tooth decay and periodontal disease.

Another exciting development is the use of cold plasma in dentistry. Recent work has shown that plasma can be an effective method of controlling oral biofilms. A biofilm (commonly known as slime) is a highly organized, three-dimensional bacterial community that enables microorganisms to communicate, maximize resources, and protect the integrity of the community. Dental plaque is an oral biofilm; it is the primary cause of both tooth decay and periodontal diseases such as Gingivitis (inflammation of the gum tissues) and Periodontitis (inflammation of the periodontium, the tissue that supports the teeth). In a laboratory environment plasma has been shown to inactivate bacteria that cause tooth decay, and periodontal diseases. Plasma has also been applied to dentin, the calcified tissue structure underneath the tooth enamel, where it was found to reduce infection. Plasma could potentially remove the infected tissue in the tooth cavity, ultimately replacing the universally feared dentist drill. These recent developments indicate that not too far in the future plasma-based devices could be available to dentists, allowing them to treat oral-borne diseases effectively, with little pain to their patients.

The authors dedicate this two-pager to the memory of Dr. Gerald (Gerry) Rogoff, who commissioned them to write it only a few months before his death. Gerry was a great scientist and a wonderful colleague.

Suggested Reading:
M. Laroussi, "Low Temperature Plasmas for Medicine?", IEEE Trans. Plasma Sci., Vol. 37, No. 6, pp. 714-725, 2009
M. G. Kong, G. Kroesen, G. Morfill, T. Nosenko, T. Shimizu, J. van Dijk and J. L. Zimmermann, "Plasma Medicine: An Introductory Review", New J. Physics, Vol. 11, 115012, 2009.

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